EXHIBIT B41

From: Jane Hall <dr.jane.hall@gmail.com>
Date: Saturday, September 29, 2018 at 12:34 AM
To: "Smith-Bindman, Rebecca" <Rebecca.Smith-Bindman@ucsf.edu>
Subject: *Re: Forest Plots - Data Decisions*

Hi Dr. Smith-Bindman,

These are our latest updates:

1. I looked into the Rosenblatt discrepancy and it looks like the odds ratios you originally provided for invasive cancer was from an all-tumors category within the same publication. I could not find any evidence of the numbers being from Terry. The updated models (linked below) use what appear to be the correct Rosenblatt invasive cancer ORs.

2. I updated the Booth "Any frequency talc use" numbers with pooled data by using the numbers reported for "rarely/weekly/monthly/daily" talc use. It was basically a mini-meta analysis with the same methods that we have been using for the main analysis. The OR and CIs are within range of those published in the other papers.

3. Based on your notes for Whittemore, (i.e. the important factor is perineal use), I believe we can use the "any perineal only" data for the "any talc" column; the smaller number of study participants who used talc for perineal and pads or diaphragms or any combination who were excluded from these OR calculations in Whittemore are likely negligible. So I added these numbers back into the analysis.

4. The updated analyses can be found in the shared file: Talc_Results.xlsx. For your reference regarding the changes to the data described above, the most updated annotated file is at september28TalcDataSummary-forAnalysisJH.xlsx.

Best,

Jane

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On Fri, Sep 28, 2018 at 10:55 AM Jane Hall <dr.jane.hall@gmail.com> wrote:
Glad to help!

I'll check on the Rosenblatt issue and let you know by email when the analyses are ready, incorporating your data updates. I think that will be this evening or tomorrow morning.

Best,

Jane
On Fri, Sep 28, 2018 at 10:51 AM Smith-Bindman, Rebecca <Rebecca.Smith-Bindman@ucsf.edu> wrote:

Jane

Thanks for reviewing data! Awesome

I took essentially all of the changes (which unfortunately will drop a bunch of data points)

Most (95%) of powder use is talc so I am less concerned if it is mixed use. And I care mostly about invasive And excluding mucionous cancer

For the Rosenblatt paper, I think I may have abstracted numbers for that study from terry is why they don't match. Can you check? Its why I had you do analysis with and without terry and Rosenblatt papers to see if it matters if they are both included (it didn't make a difference)

Thanks for updating

I will send an intro for billing

The person's name is Carmen

Best

Rebecca

From: Jane Hall <dr.jane.hall@gmail.com>
Date: Friday, September 28, 2018 at 7:42 AM
To: Rebecca Smith-Bindman <Rebecca.Smith-Bindman@ucsf.edu>
Subject: Re: Forest Plots - Data Decisions

Hi Dr. Smith-Bindman,

Here are the updates.

1. I have added a small methods write up to the first tab of TalcDataResults.xlsx, linked here.

2. I have estimated that the difference between OR and RR is negligible for the cohort study, based on the relatively percentage of disease that developed among the cohort (this is described in the methods writeup).

3. I have created an annotated file of the original talc data,linked here. Columns containing my notes are in pink cells, to the right of the original cells. Cells for your review are highlighted in yellow with text in red. I think a good portion of the data is worth checking or updating, such that it would be helpful to re-run the meta-analyses after you have made your decisions.

4. Please let me know where and how I may submit my invoice for the work completed so far.

Best,

Jane

On Thu, Sep 27, 2018 at 7:30 AM Jane Hall <dr.jane.hall@gmail.com> wrote:

Very good, I will do the first two steps and a small write up.

Best,

Jane

On Wed, Sep 26, 2018 at 7:25 AM Smith-Bindman, Rebecca <Rebecca.Smith-Bindman@ucsf.edu> wrote:

If you can estimate Or from cohort that would be awesome. It's a rare outcome so I doubt will have Any impact by would be awesome

Sent from my iPhone

On Sep 26, 2018, at 12:22 AM, Jane Hall <dr.jane.hall@gmail.com> wrote:

Hi Dr. Smith-Bindman,

Below is a link to a Dropbox file ("TalcResults.xlsx"), which contains the plots, summary statistics, and heterogeneity test results for the talc data as originally provided.

Dropbox Link to Meta-Analysis Results

With your permission, I would go ahead with a few more tasks:

- Estimating OR from RR for the cohort study, if possible.

- Checking the literature for data accuracy, and flagging discrepancies for your review.

- Checking if additional detailed raw data is available in the literature that could be used in modeling to increasing accuracy of analyses.

- (or any combination of these)

I would plan to update the results in the Dropbox file when/where relevant, so that you would continue to have access to the most accurate version.

As a progress report, I am currently at ~$1,700 of billing, in case that factors into your decision.

Best,

Jane

On Tue, Sep 25, 2018 at 5:22 PM Smith-Bindman, Rebecca <Rebecca.Smith-Bindman@ucsf.edu> wrote:

Thank you

Sent from my iPhone

On Sep 25, 2018, at 5:20 PM, Jane Hall <dr.jane.hall@gmail.com> wrote:

Hi Dr. Smith-Bindman,

Thanks for your responses!- they're very helpful.

The RR vs. OR information is interesting. For the cohort study I will estimate an odds ratio if possible. No worries about sending papers along, I have gathered those references together based on the author/year/topic information you provided.

Overall, I'm proceeding with the data as originally provided and calculating summary statistics based on an estimation of variance from the published confidence intervals, since the raw data is not available in many of the papers. There are a few assumptions here that should suffice for now to make that estimation plausible (that the data are not too skewed, that confidence intervals are roughly symmetric, and distribution is roughly normal).

This way we can have the bulk of coding done today and tomorrow, and you will have information to work off of right away. Then we can edit on a case-by-case basis as we find that any changes might needed.

I expect to send the first batch of plots and statistics this evening, but will annotate if any potential issues.

Best,

Jane

On Mon, Sep 24, 2018 at 11:42 PM Jane Hall <drjanehall@janehall-biomed.com> wrote:

Hi Dr. Smith-Bindman,

I'm partway through preparing and reviewing the data you provided, but I'm encountering some obstacles. I'm wondering how you would like me to proceed.

(I have cc'ed Ralph here in case he can offer some thoughts on what you might prefer based on his past experience with meta-analysis).

1. Missing Proportion Information. To calculate summary statistics and heterogeneity, we usually use the data that would be in a 2x2 table (i.e. N cases exposed; N cases not exposed; N controls exposed; N cases not exposed); this would apply for each of your study question columns, 1a.-1e.

a. I plan to go into the literature and access what numbers are available.

b. Where the raw numbers are not available; I would do my best to estimate, unless you have access to them and can send them to me.

c. Would it be acceptable to exclude studies from summary statistics that do not report enough information?

2. OR vs RR. Some studies (e.g. Booth 1989, Cook 1997) report adjusted relative risk ratios, not odds ratios. I'm unable to calculate the associated 95% CIs without the variance (which is not reported).

- Option 1: I could calculate unadjusted ORs for the studies that provide raw data but this is not likely to be representative of the true ORs.

- Option 2: I could run two sets of meta-analyses, one set with the literature reporting ORs, one set with RRs.

- Option 3: I could combine all study types for meta-analysis regardless, and we could accept the results within the context of an acceptable heterogeneity, and with the understanding that relative risk may considerably underestimate odds ratios.

3. Any vs. Some Talc Use. The numbers in the chart for "1a.any talc use" attributed to Booth 1989 are actually for "daily" talc use. To truly estimate "any" talc use, you may want to consider pooling the results from rarely/monthly/weekly/daily.

- Option 1: Pursue pooling data. This would require modeling the association between amounts of talc use and odds ratio, and then estimating odds ratio for "any".

- Option 2: Use data as is.

4. Invasive Cancers. Many of the numbers in column 1e (invasive cancers). are the same as in 1b (ovarian cancers). Is this intentional even though the literature (as in Cook 1997, for example) reports the odds ratio in 1e. for ovarian cancer in general, and not specifically invasive cancer?

- Option 1: I can review the data and highlight these places the table if you wish to make edits.

- Option 2: Use data as is.

By the way, do you have a preference on the following?

1. Weighting for summary statistics: I plan to use variance if available, or simply sample sizes if not all of the studies can provide enough information to do a reliable estimate of variance.

2. Fixed effects vs. random effects for summary statistics: I plan to use fixed, and add calculations for random effects if enough information is available.

3. Heterogeneity measure: I plan to use I2.

Based on your decisions, I will apply them to the remaining rows of study data for review and analyses.

Thanks,

Jane

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On Wed, Sep 19, 2018 at 3:21 PM Smith-Bindman, Rebecca <Rebecca.Smith-Bindman@ucsf.edu> wrote:

Ralph
Thanks for introduction
Jane
I am interested primarily in generating a Forrest plot with a summary estimate and test for heterogeneity

For each study I have sample size and adjusted odds ratios

Thanks
Rebecca

Sent from my iPhone